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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/754,723	01/04/2001	Suad Efendic	3745.234 US	3358

7590 11/05/2002

Steve T. Zelson, Esq.
Novo Nordisk of North America, Inc
Suite 6400
405 Lexington Avenue
New York, NY 10174-6401

EXAMINER
DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
1645	12

DATE MAILED: 11/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/754,723	Applicant(s) Efendic et al
	Examiner Patricia A. Duffy	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 13, 2002* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *15-20* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *15-20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *9*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

1. The amendment and terminal disclaimed filed 8-13-02 have been entered into the record. Claims 15-20 are pending and under examination.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

3. Any objection or rejection not reiterated herein is withdrawn based on Applicants amendments to the claims.

New Rejections Based on Amendment

4. Claims 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buckley et al (WO 91/11457) in view and Gutniak et al (Diabetologia, 33(suppl):A73, Abstract 246, 1990) of Ramachandran et al (Diabete Metabolisme, 13(2):140-141, 1987) Del Prato et al (The American Journal of Medicine, 90(suppl 6A):6A-77S, 1991) and Parker et al (Diabetes, Volume 40, Suppl 1, Abstract 847).

Buckley et al teach GLP-1 peptides, 7-34, 7-35, 7-36 and 7-37 and analogs useful for the treatment of Type II diabetes (see the claims, in particular claim 13) in particular. The analogs have amino acid substitutions at positions 7-10 and/or are truncated at the C-terminus and/or contain various other amino acid substitutions in the basic peptide and include amides. These analogs provide for an enhanced capability to stimulate insulin production or exhibit increased stability in plasma as compared to GLP-1(7-37) or both (see pages 29-33, Examples 1 and 2). Buckley et al differs by not teaching the combination with the oral hypoglycemic agents, metformin.

Gutniak et al teach that the isulinotropic effect of GLP-1 peptides are reproducible *in vivo*. Gutniak et al teach that administration to Type II diabetics decreased IMIR, stimulated insulin and inhibits glucagon and somatostatin release.

Ramachandran et al the combination of the oral hypoglycemic agents glibenclamide and metformin is effective in the treatment of Type II diabetes (see paragraph bridging pages 140-141).

Del Prato et al (The American Journal of Medicine, 90(suppl 6A):6A-77S, 1991). Del Prato et al teach that Type II diabetes (non-insulin dependent diabetes mellitus, NIDDM) appears to be a heterogenous disorder characterized by both relative insulin deficiency and impaired insulin action.

Parker et al teaches two insulin secretagogues GLP-1(7-37) and glibenclamide, an oral hypoglycemic agent, when combined had an additive effect on the amount of insulin secretion from HIT cells *in vivo*. Thus, Parker et al broadly teaches the combination of GLP-1 peptides and oral hypoglycemic agents to increase insulin secretion.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the GLP-1 peptides, 7-34, 7-35, 7-36 and 7-37 and analogs thereof as taught by Buckley et al and Gutniak et al with the oral hypoglycemic agents such as glibenclamide and metformin of Ramachandran et al to treat Type II diabetes because Parker et al teach that the GLP-1 and glibenclamide when combined had an additive effect on the amount of insulin secretion and therefore the combination of the agents would be reasonably expected to be useful in the treatment of Type II diabetes. One would have been further motivated to combine the GLP-1 with metformin and glibenclamide because Del Prato teach that Type II diabetes is a heterogenous disorder characterized by relative insulin deficiency and impaired insulin action and the combination

of GLP-1 with the oral hypoglycemic agents would be reasonably expected to further increase the endogenous insulin levels and therefore be useful in the treatment of Type II diabetes and further, one skilled in the art would have a reasonable expectation of success because Gutniak et al that demonstrates that the in *vitro* pharmacology of GLP-1 correlates with the *in vivo* actions.

Response to Arguments

5. Applicants arguments are moot in view of the new rejection set forth above.

Status of Claims

6. All claims stand rejected.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

8. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Thursday and Saturday from 10:30 AM to 7:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
November 4, 2002

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600